Therapeutic Management of Lennox-Gastaut Syndrome

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Challenges in Managing LGS

- Polymorphic Intractable seizure Types
- Different Etiologies
- Cognitive and Behavioral Abnormalities
- High Incidence of Status Epilepticus
- Broad range of Comorbid Conditions
Principle of Antiepileptic treatment

LGS

- Seizures associated with LGS are highly resistant to AED treatment
- Often needs Polypharmacy
- Overtreatment with antiepileptic drugs is common
- Tonic seizures are the most difficult to treat
- Transient beneficial Effects
**Treatment Goals for Epilepsy**

**Newly Diagnosed**
- AED Trial 1 Monotherapy

**Refractory Epilepsy**
- Video EEG
  - Epilepsy Surgery
  - VNS Therapy
  - AEDs (Polytherapy)
  - Ketogenic Diet

**AED Trial 1 Monotherapy**
- Treatment Goal: Seizure freedom

**Newly Diagnosed**
- Treatment Goal: Maximize QoL
  - Long-term seizure control
  - Minimize AED side effects
  - Maximize adherence

**Refractory Epilepsy**
- Treatment Goal: Maximize QoL

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Drug Development in LGS

- A few randomized, double blind, placebo-controlled trials of single agents have been performed in LGS.

- Studies varied considerably in their experimental design and patient selection criteria.

- No head-to-head trial comparing more than one drug have been published.
Dimensions of Treatment in LGS

Overall quality of life is a fundamental measure of successful treatment in patients with epilepsy.

Valproic Acid

- Valproic acid is considered the most useful initial medication of choice for drop attacks, atypical absences and myoclonic seizures in LGS
- There are no controlled studies for valproic acid
- Caution must be exercised in using valproic acid in children under the age of 2 years to prevent hepatotoxicity.
New Generation of Treatments for LGS

- felbamate, lamotrigine, topiramate, rufinamide and Clobosam are the antiepileptic medications with an indication to treat seizures associated with LGS.
Benzodiazepines

- The effects of benzodiazepines are variable. A recent study showed that clobazam significantly reduced both drop and non-drop seizures in a dose-dependent manner in patients with LGS.
- Clobazam reportedly has less sedative effects than other benzodiazepines, making it an attractive potential adjunctive treatment for LGS.
Felbamate

- Felbamate could also be considered as an alternative to valproic acid, because felbamate lacks the sedative side effect seen with other anticonvulsants.
- Caretakers must be provided detailed information about the potential risks of felbamate. They need to understand the risk of aplastic anemia and hepatic toxicity with felbamate use, this medication must be used with caution and appropriate patient monitoring of blood levels, liver function, and hematologic indices.
Suggested Treatment Sequence

1st AED Trial → 2nd AED Trial → Polytherapy AED Trial

Refractory Epilepsy Evaluation

- Surgery Appropriate
  - Proceed
    - Not Seizure Free
      - Reevaluate VNS
    - Seizure Free

- Surgery Not Appropriate
  - VNS Therapy
    - Not Improved
      - Reevaluate ES
    - Improved
      - Continued VNS

Non-Pharmacological Treatments

LGS

- Vagus Nerve Stimulation
- Epilepsy Surgery
- Ketogenic Diet
- Immunomodulation IVIG (Intravenous Immunoglobulin)
Epilepsy Surgery Evaluation

EEG & video-EEG
MRI & CT
PET & SPECT

History
Exam
Neuropsychologic test
Neuropsychiatry
Wada (Intracarotid amobarbital test)
Social work evaluation

Invasive EEG  Pathophysiology/Syndromes  MEG - source localization
Epilepsy Surgery
Resective Surgery

• Often Multifocal
• Poorly lateralized
• Deep Frontal Regional onset
• Not Ideal surgical Candidate
Epilepsy Surgery
Corpus Callosotomy

- Indicated for devastating Atonic seizures.
- May help prevent Convulsive Status Epilepticus
- Anterior two-thirds sections, may be sufficient
- Seizures may return
Vagus nerve stimulator
- Setting and adjusting VNS Therapy’s dosing is done using a handheld computer and a programming wand.
- After a progressive ramping-up of the output current, the typical parameters are

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<th>Typical</th>
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<td>Output current</td>
<td>Milliamps (mA)</td>
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<td>1 - 2</td>
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<tr>
<td>Signal frequency</td>
<td>Hertz (Hz)</td>
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<td>20 - 30</td>
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<td>Pulse width</td>
<td>Microseconds (µsec)</td>
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<td>Signal ON time</td>
<td>Seconds (sec)</td>
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<tr>
<td>Signal OFF time</td>
<td>Minutes (min)</td>
<td>0.2 – 180</td>
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Ketogenic Diet
Ketogenic Diet
Role in seizure control
Ketogenic Diet
Non-Convulsive Status Epilepticus

- Mixed Tonic and Absence Status is the most common type.
- Profound Impairment of Consciousness or Stupor
- May be missed if not suspected
- For Impending Status, Rectal diazepam or an oral intake of a high dose of clobazam can stop serial attacks.
- Medical Emergency
Management Tips
Lennox–Gastaut Syndrome

- With increasing seizures, reducing medications may be a better option than increasing.
- For Medication selection: Target the predominant, severe and disabling seizure type.
- Medication changes can be challenging.
- Cognitive Impairment may worsen with complex polypharmacy.
Management Tips
Lennox–Gastaut Syndrome Cont.

• Attention to Seizure Precipitants
• A multidisciplinary approach is required
• Treat Behavior Difficulties, many develop behavioral problems (hyperactivity, and aggression)
• Develop a Care plan and Rescue Treatment
• A specialist should follow LGS patients
• New treatment options with milder side effects may improve the quality of life for these patients.
Thank you